CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

SJIF Impact Factor: 7.187

https://doi.org/10.5281/zenodo.17443881

https://www.iajps.com/volumes/volume12-october-2025/116-issue-10-october-25/

Available online at: http://www.iajps.com *Research Article*

FORMULATION DEVELOPMENT AND EVALUATION OF MUCOADHESIVE BUCCAL TABLETS OF NARATRIPTAN

Shireen Fatima[1], Dr. Abdul Sayeed[2], Dr. Syed Areefulla Hussainy[2] Dr. Faizan Sayeed[2]

[1].Research Scholar Mesco College of Pharmacy, Hyderabad.

[2].Professor, Mesco College of Pharmacy, Hyderabad.

Abstract:

The present study was aimed at the formulation development and evaluation of mucoadhesive buccal tablets of Naratriptan to enhance its bioavailability and therapeutic efficacy in the treatment of migraine. Naratriptan undergoes extensive first-pass metabolism, resulting in reduced oral bioavailability; hence, buccal delivery was chosen as an alternative route to bypass hepatic metabolism and provide sustained drug release. Mucoadhesive buccal tablets were prepared using various natural and synthetic polymers such as Sodium starch glycolate, Crospovidone and Croscarmellose sodium by direct compression method.

The formulations were evaluated for pre-compression parameters (bulk density, tapped density, angle of repose) and post-compression parameters (hardness, thickness, friability, drug content, surface pH, swelling index, mucoadhesive strength, and in vitro drug release). All evaluation parameters were found within the acceptable limits. Among the developed formulations, F4 was identified as the optimized formulation, showing a maximum drug release of 99.72 % over 8 hours along with excellent mucoadhesive properties and sustained release profile. The results of this study indicate that mucoadhesive buccal tablets of Naratriptan offer a promising approach for improving bioavailability and achieving prolonged therapeutic effect in migraine therapy.

Keywords: Naratriptan , Sodium starch glycolate, Crospovidone and Croscarmellose

Corresponding author:

Shireen Fatima,

M.Pharm

Mesco college of Pharmacy,

Email Id:fatimashireenismathiya@gmail.com

QR CODE

Please cite this article in press Shireen Fatima et al., ***Formulation Development And Evaluation Of Mucoadhesive Buccal Tablets Of Naratriptan****, Indo Am. J. P. Sci, 2025; 12(10).*

1. INTRODUCTION [1-20]

Buccal delivery of drugs provides an attractive alternative to the oral route of drug administration, particularly in overcoming deficiencies associated with the latter mode of dosing .Problems such as first pass metabolism and drug degradation in the GIT environment can be circumvented by administering the drug via buccal route. Moreover, the oral cavity is easily accessible for self medication and be promptly terminated in case of toxicity by removing the dosage form from buccal cavity. It is also possible to administer drugs to patients who cannot be dosed orally via this route Successful buccal drug delivery using buccal adhesive system requires at least three of the following (a) A bioadhesive to retain the system in the oral cavity and maximize the intimacy of contact with mucosa (b) A vehicle the release the drug at an appropriate rate under the conditions prevailing in the mouth and (c) Strategies for overcoming the low permeability of the oral mucosa. Buccal adhesive drug delivery stem promote the residence time and act as controlled release dosage forms.

The use of many hydrophilic macromolecular drugs as potential therapeutic agents is their in adequate and erratic oral absorption. However, therapeutic potential of these compounds lies in our ability to design and achieve effective and stable delivery systems. Based on our current understanding, it can be said that many drugs cannot be delivered effectively through the conventional oral route.

The main reasons for the poor bio-availability of many drugs through conventional oral route are:

- ✓ Pre-systemic clearance of drugs.
- ✓ The sensitivity of drugs to the gastric acidic environment which leads to gastric irritation. Limitations associated with gastro intestinal tract like variable absorption characteristics.

Buccal mucosa composed of several layers of different cells. The Epithelium is similar to stratified squamous epithelia found in rest of the at least one of which is biological nature are held together by means of interfacial forces.[1]

Buccal drug delivery is a type of bioadhesive drug delivery especially it is a mucoadhesive drug delivery system is adhered to buccal mucosa.

The term bioadhesion is commonly defined as an adhesion between two materials where at least one of the materials is of biological origin. In the case of bio adhesive drug delivery systems, bioadhesion often refers to the adhesion between the excipients of the formulation (i.e. the inactive media) and the biological tissue.

The term mucoadhesion can be considered to refer to a sub group of bioadhesion and, more specifically, to the case when the formulation interacts with the mucous layer that covers a mucosal tissue.

The mucosal layer lines a number of regions of the body including gastrointestinal tract, urogenital tract, airway, ear, nose and eye. Hence mucoadhesive drug delivery system includes the following:

1. Buccal delivery system
2. Oral delivery system
3. Ocular delivery system
4. Vaginal delivery system
5. Rectal delivery system
6. Nasal delivery system[2]

Ideal Characteristics of Buccal Drug Delivery System

- ✓ Should adhere to the site of attachment for a few hours.
- ✓ Should release the drug in a controlled fashion.
- ✓ Should provide drug release in a unidirectional way toward the mucosa.
- ✓ Should facilitate the rate and extent of drug absorption.
- ✓ Should not cause any irritation or inconvenience to the patient.
- ✓ Should not interfere with the normal functions such as talking and drinking.

ADVANTAGES OF BUCCAL DRUG DELIVERY SYSTEM

1) Bypass the gastrointestinal tract and hepatic portal system, increasing the bioavailability of orally administered drugs that otherwise undergo hepatic first-pass metabolism. In addition the drug is protected from degradation due to pH and digestive enzymes of the middle gastrointestinal tract.

2) Improved patient compliance due to the elimination of associated pain with injections; administration of drugs in unconscious or incapacitated patients; convenience of administration as compared to injections or oral medications.

3) Sustained drug delivery.
4) A relatively rapid onset of action can be achieved relative to the oral route, and the formulation can be removed if therapy is required to be discontinued.

5) Increased ease of drug administration.

DISADVANTAGES OF BUCCAL DRUG DELIVERY SYSTEM

1) Low permeability of the buccal membrane: specifically when compared to the sublingual membrane.

2) Smaller surface area. The total surface area of membranes of the oral cavity available for drug absorption is 170 cm2 of which ~50 cm^2 represents non-keratinized tissues, including the buccal membrane.

3) The continuous secretion of saliva (0.5–2 l/day) leads to subsequent dilution of the drug.

4) Swallowing of saliva can also potentially lead to the loss of dissolved or suspended drug and, ultimately, the involuntary removal of the dosage form.

These are some of the problems that are associated with buccal drug delivery.

LIMITATIONS OF BUCCAL DRUG ADMINISTRATION

1) Drugs which are unstable at buccal pH cannot be administered.

2) Eating and drinking may become restricted.

3) There is an ever present possibility of the patient swallowing the dosage form.

4) Over hydration may leads to slippery surface and structural integrity of the formulation may get disrupted by this swelling and hydration of the bioadhesive polymers.

5) Drugs which irritate the mucosa or have a bitter or unpleasant taste or an obnoxious odor cannot be administered by this route.

2.METHODOLOGY [21-40]

PREFORMULATION STUDIES

Drug-excipient compatibility studies

Fourier Transform Infrared spectroscopic studies

A Fourier Transform – Infra Red spectrophotometer was used to study the non-thermal analysis of drug-excipient (binary mixture of drug: excipient 1:1 ratio) compatibility. The spectrum of each sample was recorded over the 450-4000 cm^{-1}. Pure drug of Naratriptan, Naratriptan with physical mixture (excipients) compatibility studies were performed.

Analytical Method Used in the Determination of Naratriptan

Preparation of 0.2M Potassium Dihydrogen Orthophosphate Solution: Accurately weighed 27.218 gm of monobasic potassium dihydrogen orthophosphate was dissolved in 1000 mL of distilled water and mixed.

Preparation of 0.2M sodium hydroxide solution: Accurately weighed 8 gm of sodium hydroxide pellets were dissolved in 1000 mL of distilled water and mixed

Preparation of pH 6.8 phosphate buffer: Accurately measured 250 mL of 0.2M potassium dihydrogen ortho phosphate and 112.5 mL of 0.2M NaOH was taken into the 1000 mL volumetric flask. Volume was made up to 1000 mL with distilled water.

Preparation of standard graph in phosphate buffer pH 6.8

100 mg of Pure Drug was dissolved in small amount of Methanol (5-10 ml), allowed to shake for few minutes and then the volume was made up to 100ml with phosphate buffer pH 6.8, from this primary stock (1mg/ml), 10 ml solution was transferred to another volumetric flask made up to 100 ml with phosphate buffer pH 6.8. From this secondary stock 0.5, 1.0, 1.5, 2.0, 2.5, ml was taken separately and made up to 10 ml with phosphate buffer pH 6.8 to produce 5, 10, 15, 20, 25 µg/ml respectively. The absorbance was measured at 282 nm using a UV spectrophotometer. Standard calibration curve values were shown in Table 1. The standard calibration curve of Naratriptan in phosphate buffer pH 6.8 was shown in fig .

Solubility Studies

The solubility of Naratriptan in phosphate buffer solution pH 6.8 was determined by phase equilibrium method. An excess amount of drug was taken into 20 ml vials containing 10 ml of phosphate buffers (pH 6.8). Vials were closed with rubber caps and constantly agitated at room temperature for 24 hr using rotary shaker. After 24 hr, the solution was filtered through 0.2µm Whattman's filter paper. The amount of drug solubilized was then estimated by measuring the absorbance at 282 nm using a UV spectrophotometer.

The standard curves for Naratriptan were established in phosphate buffers (pH 6.8) and from the slope of the straight line the solubility of Naratriptan was calculated. The studies were repeated in triplicate (n = 3), and mean was calculated.

***Ex-vivo* permeation studies through porcine buccal mucosa**

The aim of this study was to investigate the permeability of buccal mucosa to Naratriptan. It is based on the generally accepted hypothesis that the epithelium is the rate-limiting barrier in the buccal absorption.

A Tissue permeation

Buccal tissue was taken from Pigs slaughter-house. It was collected within 10 minutes after slaughter of

pig and tissue was kept in Krebs buffer solution. It was transported immediately to the laboratory and was mounted within 2hrs of isolation of buccal tissue. The tissue was rinsed thoroughly using phosphate buffer saline to remove the adherent material. The buccal membrane from the tissue was isolated using surgical procedure. Buccal membrane was isolated and buccal epithelium was carefully separated from underlying connective tissue. Sufficient care was taken to prevent any damage to the epithelium.

Table 1.: Composition of Tyrode solution (Krebs buffer)

Ingredients	Quantity(gm)
Sodium chloride	8.0
Potassium chloride	0.2
Calcium chloride dehydrate	0.134
Sodium bicarbonate	1.0
Sodium dihydrogen orthophosphate	0.05
Glucose monohydrate	1.0
Magnesium chloride	0.1
Distilled water up to	1.0Litre

b. Procedure for calibration curve of phenol red:
Various stock solutions of phenol red at concentrations ranging from 50µg/mL to 1µg/mL were prepared with phosphate buffer pH 6.8, 0.5 mL of Acetonitrile was added and vortexed. This was followed by addition of 2mL of 0.2M NaoH, mixed well and volumes were made up to 10 mL with distilled water and were centrifuged. The resulting final concentration ranged from 2.5µg/mL to 25µg/mL. The absorbance was measured at 536 nm and standard graph was plotted.

c. *Ex-vivo* permeation of drug solution
Ex-vivo permeation study of Naratriptan through the porcine buccal mucosa was performed using Franz diffusion cell and membrane assembly, at 37°C ± 0.2°C and 50 rpm. This temperature and rpm were maintained by magnetic stirrer. Porcine buccal mucosa was obtained from a local slaughterhouse and used within 2hr of slaughter. The tissue was stored in Krebs buffer at 4°C upon collection. After the buccal membrane was equilibrated for 30 min with the buffer solution between both the chambers, the receiver chamber was filled with fresh buffer solution (pH 7.4), and the donor chamber was charged with 5mL (1mg/mL) of drug solution. Aliquots (5mL) were collected at predetermined time inter wells up to 6hr and the amount of drug permeated through the buccal mucosa was then determined by measuring the absorbance at 282 nm using a UV spectrophotometer. The medium of the same volume (5mL), which was pre-warmed at 37°C, was then replaced into the receiver chamber. The experiments were performed in triplicate (n = 3) and mean values were used to calculate flux (J) and permeability coefficient (P).

$$J = \frac{(dQ/dt)}{A}$$

$$P = \frac{(dQ/dt)}{\Delta CA}$$

Where, J is Flux ($mg.hrs^{-1}cm^{-}$P is permeability coefficient (cm/h) dQ/dt is the slope obtained from the steady state portion of the curve ΔC is the concentration difference across the mucosa and A the area of diffusion (cm^2)

Formulation development of tablets
Buccal tablets were prepared by a direct compression method, before going to direct compression all the ingredients were screened through sieve no.100. Acritamer 940, Manugel and Hypromellose K100M are the mucoadhesive and biodegradable polymers used in this preparation of buccal mucoadhesive drug delivery systems.

Naratriptan was mixed manually with different ratios of Acritamer 940, Manugel and Hypromellose K100M and Microcrystalline Cellulose as diluent for 10 min. The blend was mixed with talc and magnesium stearate for 3-5 min.

Evaluation of Pre-Compression Blend:
The quality of tablet, once formulated, by rule is generally dictated by the quality of physicochemical properties of blends. There are many formulations and process variables involved in mixing and all these can affect the characterization of blends produced. Prior to compression, granules were evaluated for their characteristic parameter such as Tapped density, Bulk density, Carr's index, Angle of repose, Hausner's ratio. Compressibility index was calculated from the bulk and tapped density using a digital tap density apparatus. The various characteristics of blends tested are as given below:

a) Angle of repose:
The angle of repose of granules was determined by the funnel method. The accurately weighed granules were taken in a funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touches the apex of the heap of the granules. The granules were allowed to flow through funnel freely onto the surface. The diameter of the

powder cone was measured and angle of repose was calculated using the following equation:

$$\tan\theta = h/r$$

Where, θ = angle of repose

h = height of the cone

r = radius of the cone base

The relationship between the angle of repose and flowability is as follows:

S.No	Angle of Repose	Flowability
1.	<25	Excellent
2.	25-30	Good
3.	30-40	Passable
4.	>40	Poor flow

Table2. Angle of repose values

b) Bulk density:

Density is defined as weight per unit volume. Bulk density ρb, is defined as the mass of the powder divided by the bulk volume and is expressed as gm/cm^3. The bulk density of a powder primarily depends on particle size distribution, particle shape and the tendency of particles to adhere together. Bulk density is very important in the size of containers needed for handling, shipping and storage of raw material and blend. It is also important in size blending equipment. 30 gm of powder blend introduced into a dry 100 mL cylinder, without compacting. The powder was carefully leveled without compacting and the unsettled apparent volume V_0, was read. The bulk density was calculated using the formula:

$$\rho b = M/V_0$$

Where, ρb= Apparent bulk density.

M=Weight of the sample.

V=Apparent volume of powder.

c) Tapped density:

After carrying out the procedure as given in the measurement of bulk density the cylinder containing the sample was tapped using a suitable mechanical tapped density tester that provides a fixed drop of 14±2 mm at a nominal rate of 300 drops per minute. The cylinder was tapped 500 times initially followed by an additional tap of 750 times until difference between succeeding measurement is less than 2% and then tapped volume, V_f was measured, to the nearest graduated unit. The tapped density was calculated, in gm per mL, using the formula:

$$\rho_{tap} = M/V_f$$

Where, ρ_{tap}= Tapped density.

M = Weight of the sample.

V_f= tapped volume of the powder.

d) Carr's index:

The compressibility index (Carr's index) is a measure of the propensity of a powder to be compressed. It is determined from the bulk and tapped densities. In theory, the less compressible a material the more flowable it is. As such, it is measure of the relative importance of interparticulate interactions. In a free-flowing powder, such interactions are generally less significant, and the bulk and tapped densities will be closer in value. For poorer flowing materials, there are frequently greater interparticle interactions, and a greater difference between the bulk and tapped densities will be observed. These differences are reflected in the compressibility index which is calculated using the following formula:

$$\text{Carr's index} = [(\rho_{tap}-\rho b)]/\rho_{tap}]\times 100$$

Where, ρb= bulk density

ρ_{tab}= tapped density

Table3.Carr's index values

S. No	Carr's Index	Flowability
1.	5-12	Free Flowing
2.	13-16	Good
3.	18-21	Fair to Passable
4.	23-35	Poor
5.	33-38	Very Poor
6.	>40	Extremely Poor

e) Hausner's ratio:

It is the ratio of tapped density to the bulk density. Hausner found that this ratio was related to interparticle friction and, as such, could be used to predict powder flow properties. Generally, a value less than 1.25 indicates good flow properties, which is equivalent to 20% of Carr's index.

$$\text{Hausner's Ratio} = \rho_{tap}/\rho b$$

Where, ρ_{tap} = Tapped density.

ρb = Bulk density.

S.No	Hausner's Ratio	Flowability
1.	0-1.2	Free flowing
2.	1.2-1.6	Cohesive powder

Table.4Hausner's ratio values

Preparation of Tablets:
Then the powder blend was compressed into tablets by the direct compression method using 6mm flat faced punches. The tablets were compressed using a sixteen station LAB PRESS rotary tablet-punching machine. The weights of the tablets were determined using a digital balance and thickness with digital screw gauge. Composition of the prepared bioadhesive buccal tablet formulations of Naratriptan were given in Table10

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Naratriptan	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Sodium starch glycolate	2.5	5	7.5	-	-	-	-	-	-
Crospovidone	-	-	-	2.5	5	7.5	-	-	-
Croscarmellose sodium	-	-	-	-	-	-	2.5	5	7.5
Magnesium stearate	2	2	2	2	2	2	2	2	2
Talc	2	2	2	2	2	2	2	2	2
Microcrystalline cellulose	QS	QS	QS	QS	QS	QS	QS	QS	QS
Total Weight (mg)	60	60	60	60	60	60	60	60	60

RESULTS AND DISCUSSION:

Solubility Studies:

Table 5. Solubility studies

S.No	Medium	Amount present (µg/mL)
1	Phosphate pH 6.8 buffer	96.92
2	Phosphate pH 7.4 buffer	91.14

Saturation solubility of Naratriptan in various buffers were studied and shown in the Table 5. The results revealed that the solubility of the Naratriptan was increased from pH 6.8 to 7.4. The solubility of the Naratriptan in phosphate buffer pH 6.8 is 96.92µg/mL and it was selected as the suitable media for the release studies because the pH of the phosphate buffer pH 6.8 is nearer to that of buccal mucosa pH.

Standard graph in phosphate buffer pH 6.8 (λ_{max} 255 nm)
Standard graph of Naratriptan was plotted as per the procedure in experimental method and its linearity is shown in Table 5 and Fig 1 **.** The standard graph of Naratriptan showed good linearity with R^2 of 0.999, which indicates that it obeys "Beer- Lamberts" law.

Table 6 : Standard graph values of Naratriptan in pH 6.8 phosphate buffer

Concentration (µg/mL)	Absorbance
0	0
5	0.158
10	0.304
15	0.449
20	0.587
25	0.717

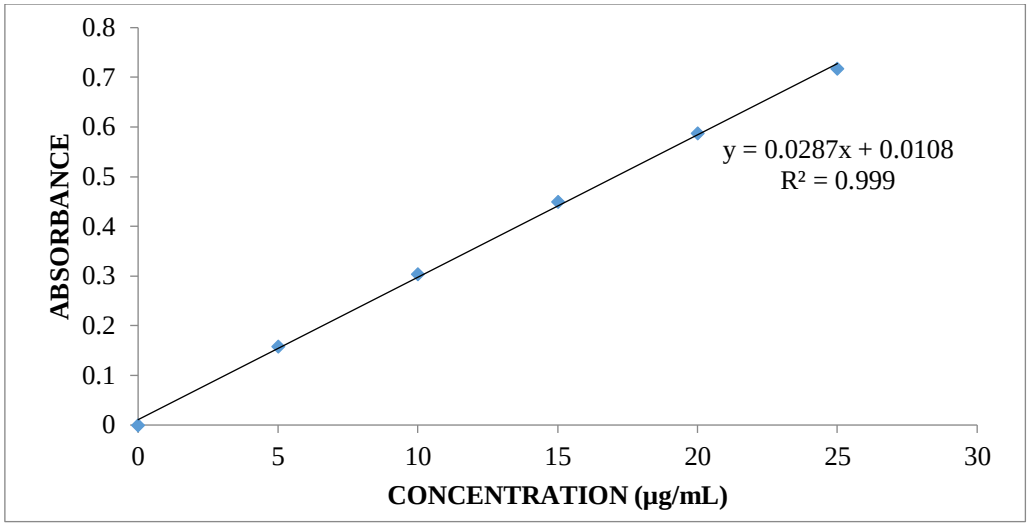

Fig 1 Standard graph of Naratriptan in pH 6.8 phosphate buffer

Standard graph in phosphate buffer pH 7.4 (λ_{max} 257 nm)

Standard graph of Naratriptan was plotted as per the procedure in experimental method and its linearity is shown in Table 6 and Fig .2. The standard graph of Naratriptan showed good linearity with R^2 of 0.999, which indicates that it obeys "Beer- Lamberts" law.

Table 7.: Standard graph values of Naratriptan in pH 7.4 phosphate buffer

Concentration (µg/mL)	Absorbance
0	0
5	0.127
10	0.252
15	0.368
20	0.482
25	0.598

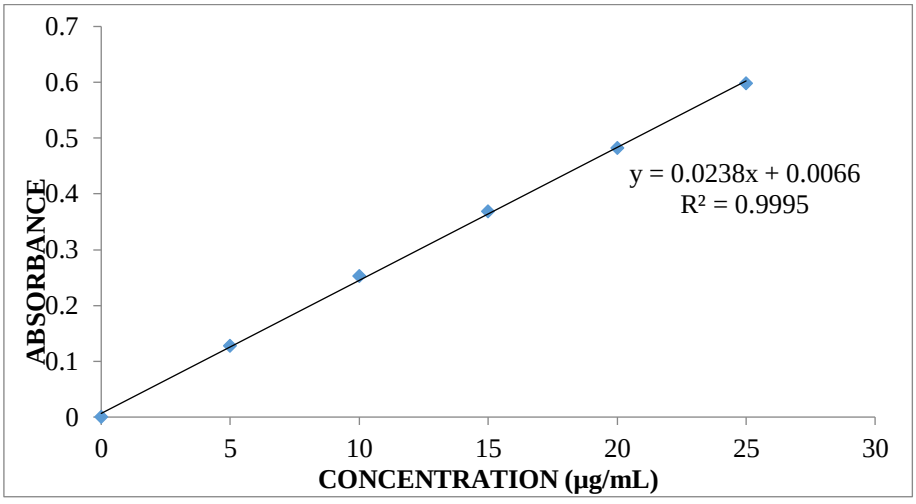

Fig : 8 Standard graph of Naratriptan in pH 7.4 phosphate buffer

Evaluation:

Characterization of pre-compression blend: Tablet powder blend was subjected to various pre-formulation parameters. The angle of repose values indicates that the powder blend has good flow properties. The bulk density of all the formulations was found to be in the range of 0.41 to 0.50 (gm/cm^3) showing that the powder has good flow properties. The tapped density of all the formulations was found to be in the range of 0.50 to 0.58 showing the powder has good flow properties. The compressibility index of all the formulations was found to be below

18.8 which show that the powder has good flow properties. All the formulations has shown the Hausner's ratio below 1.22 indicating the powder has good flow properties.

Table 9 : Physical properties of pre-compression blend

Formulation Code	Angle of repose (Θ)	Bulk density (gm/cm^3)	Tapped density (gm/cm^3)	Carr's Index (%)	Hausner's ratio
F1	26.2	0.45	0.55	18.1	1.22
F2	25.4	0.47	0.55	14.5	1.17
F3	26.8	0.50	0.58	13.7	1.16
F4	24.8	0.46	0.55	16.3	1.19
F5	24.3	0.50	0.58	13.7	1.16
F6	26.3	0.47	0.55	14.5	1.17
F7	26.4	0.50	0.58	13.7	1.16
F8	24.3	0.41	0.50	18.6	1.21
F9	28.4	0.41	0.50	18.8	1.21

Evaluation of buccal tablets:

Physical evaluation of Naratriptan buccal tablets: The results of the weight variation, hardness, thickness, friability and drug content of the tablets are given in Table 10 All the tablets of different batches complied with the official requirement of weight variation as their weight variation passes the limits. The hardness of the tablets ranged from 4.0 to 4.9 kg/cm^2 and the friability values were less than 0.62 % indicating that the buccal tablets were compact and hard. The thickness of the tablets ranged from 3.20 – 3.97 mm. All the formulations satisfied the content of the drug as they contained 96.21-99.96 % of Atenolol. Thus all the physical attributes of the prepared tablets were found to be practically within control limits.

Table 10: Physical evaluation of Naratriptan buccal tablets

Formulation code	Weight variation (mg)	Thickness (mm)	Hardness (Kg/cm^2)	Friability (%)	Content uniformity (%)
F1	59.34	1.97	2.6	0.56	99.64
F2	60.14	1.81	2.2	0.34	98.90
F3	58.92	1.64	2.0	0.28	99.96
F4	57.37	1.90	2.2	0.62	96.21
F5	59.50	1.76	2.8	0.59	97.89
F6	56.83	1.64	2.1	0.46	98.16
F7	60.09	1.20	2.9	0.61	97.62
F8	57.21	1.69	2.3	0.50	98.89
F9	58.64	1.49	2.7	0.45	99.41

Swelling Index

Table11 : Swelling Index and Mucoadhesive strength (G)

S.NO.	Formulations	Swelling Index (%)	Mucoadhesive strength(G)
1	F1	0.81	11.21±2.72
2	F2	1.01	13.03±0.94
3	F3	2.14	14.16±2.83
4	F4	2.53	16.60±0.64
5	F5	2.46	10.02±2.26
6	F6	2.40	10.14±3.79
7	F7	0.80	12.62±2.15
8	F8	1.19	14.29±0.67
9	F9	2.31	15.32±1.90

Swelling index is an important parameter in judging the mucoadhesion property, at least in the initial stages, since water uptake is important for the polymers to uncoil and interact with the mucin.

The swelling indices of the Naratriptan buccal tablets reveals that while the buccal tablet formulations are all made of different materials, the extent of swelling differs based on the individual tablet composition.

The Swelling indices of the first three formulations are quite low because of the fact that they started to disintegrate and lose mass soon after placing them upon the Petri-dish. The formulations containing lower levels of the polymers Chitosan displayed the highest swelling index.

***In vitro* release studies:**

In vitro drug release studies were conducted in phosphate buffer pH 6.8 and the studies revealed that the release of Naratriptan from different formulations varies with characteristics and composition of matrix forming polymers.

Table 12: *In vitro* dissolution data for formulations F1 – F9

TIME (H)	CUMULATIVE PERCENTE OF DRUG RELEASE								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
0.5	26.15	19.10	14.98	31.57	25.63	15.96	27.56	21.90	18.29
1	39.62	24.53	18.60	47.49	30.75	25.48	35.43	28.53	22.02
2	46.98	38.86	23.54	52.26	47.14	26.41	42.29	35.16	28.96
3	50.83	47.54	39.72	60.52	53.60	33.24	52.59	46.24	35.10
4	66.47	55.99	45.34	76.14	67.59	48.67	65.63	65.97	41.57
5	79.68	67.42	50.75	85.38	70.37	53.68	70.15	71.24	57.98
6	85.89	74.27	66.18	88.89	75.10	62.11	85.66	78.85	62.31
7	92.50	89.38	72.26	94.14	88.81	76.93	90.34	82.31	78.92
8	96.76	94.18	88.74	99.72	91.98	86.54	96.24	91.73	87.06

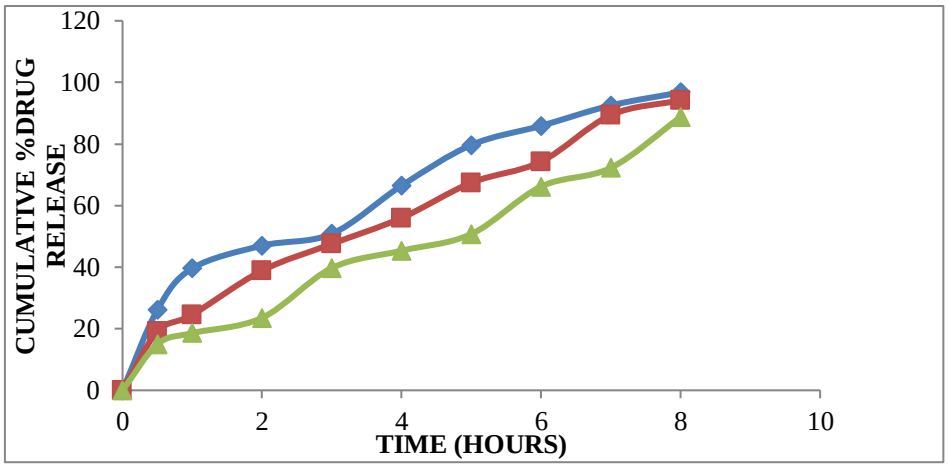

Fig 3: *In vitro* dissolution data for formulations F1 – F3 by using Sodium starch glycolate polymer

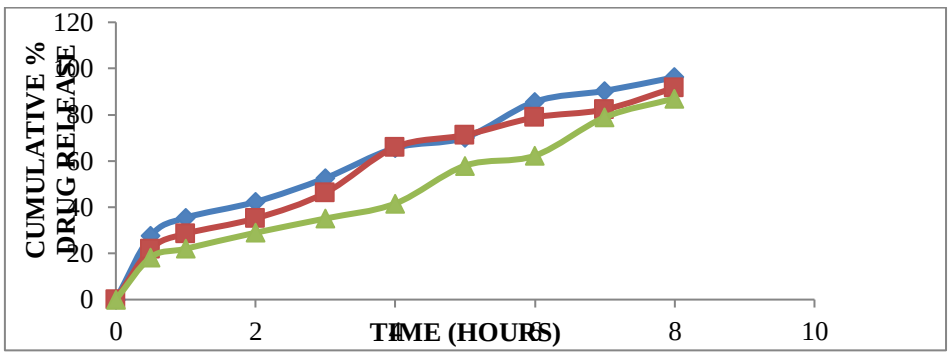

Fig4 : *In vitro* dissolution data for formulations F4 –F6 by using Crospovidone polymer

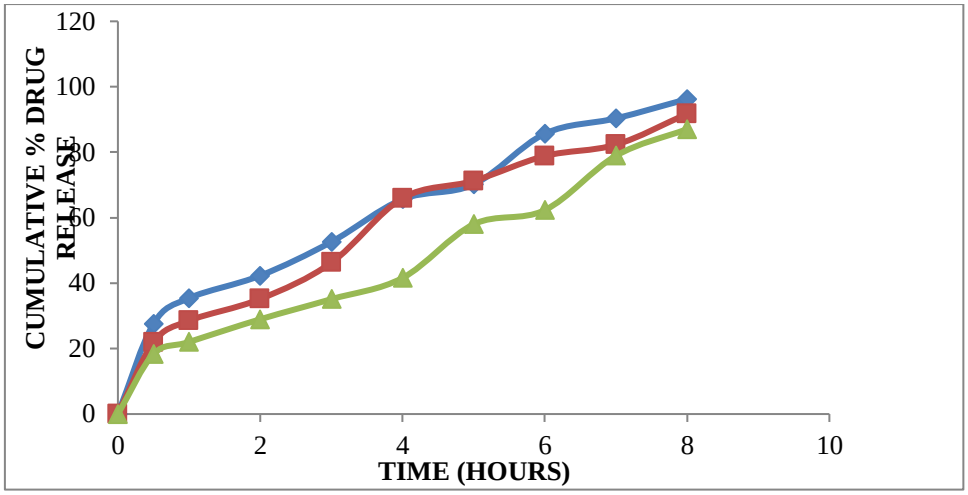

Fig :5 *In vitro* dissolution data for formulations F7 –F9 by using Croscarmellose sodium polymer

From the dissolution studies observed Total nine Formulations are prepared. The formulations prepared with Sodium starch glycolate in different concentrations. The formulation F1 was maximum drug released 96.76 % in 8 h. Concentration of polymer increased the drug release was decreased.

The formulation was prepared with Crospovidone the drug release was observed, the formulation F4 was showed 99.72 % maximum drug release in 8 hours.

The formulation was prepared with Croscarmellose sodium the drug release was observed, the formulation F7 was showed 96.24 % maximum drug release in 8 hours.

Among all formulations F4 was showed maximum drug release in 8 hrs. So, Formulation F4 was selected as optimized formulation.

Table :13 Moisture absorption, surface pH of selected formulations

Formulation Code	Moisture absorption	Surface pH
F1	90	6.12
F4	95	5.82
F7	93	6.08

The moisture absorption studies give important information of the relative moisture absorption capacities of polymers and it also give information regarding whether the formulations maintain the integrity or not. Among the selected formulations F4 formulation shown good moisture absorption.

The surface pH of the buccal tablets was determined in order to investigate the possibility of any side effects. As an acidic or alkaline pH may cause irritation to the buccal mucosa, it was determined to keep the surface pH as close to neutral as possible. The surface pH of the selected formulations was found to be 5.82 to 6.12 and the pH was near to the neutral. These results suggested that the polymeric blend identified was suitable for oral application and formulations were not irritant to the buccal mucosa.

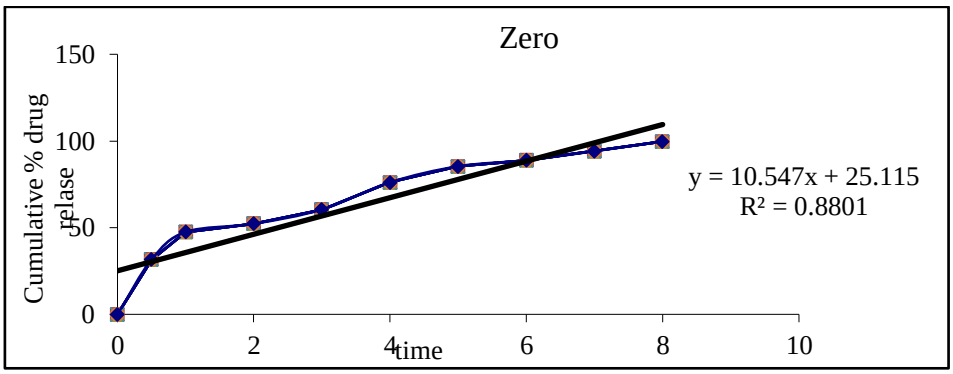

Fig 6: Zero order plot of optimized formulation

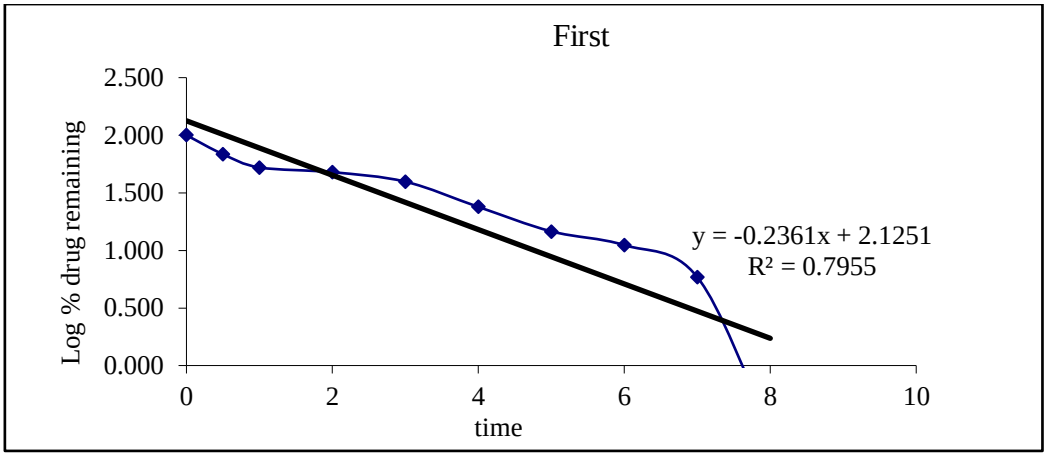

Fig :7 First order plot of optimized formulation

This formulation was following Higuchi release mechanism with regression value of 0.984.

Drug – excipient compatibility studies by physical observation:

Naratriptan was mixed with various proportions of excipients showed no colour change at the end of two months, proving no drug-excipient interactions.

FTIR

FTIR spectra of the drug and the optimized formulation were recorded. The FTIR spectra of pure Naratriptan drug, drug with polymers (1:1) shown in the below figures respectively. The major peaks which are present in pure drug Naratriptan are also present in the physical mixture, which indicates that there is no interaction between drug and the polymers, which confirms the stability of the drug. There was no disappearance of any characteristics peak in the FTIR spectrum of drug and the polymers used. This shows that there is no chemical interaction between the drug and the polymers used. The presence of peaks at the expected range confirms that the materials taken for the study are genuine and there were no possible interactions.

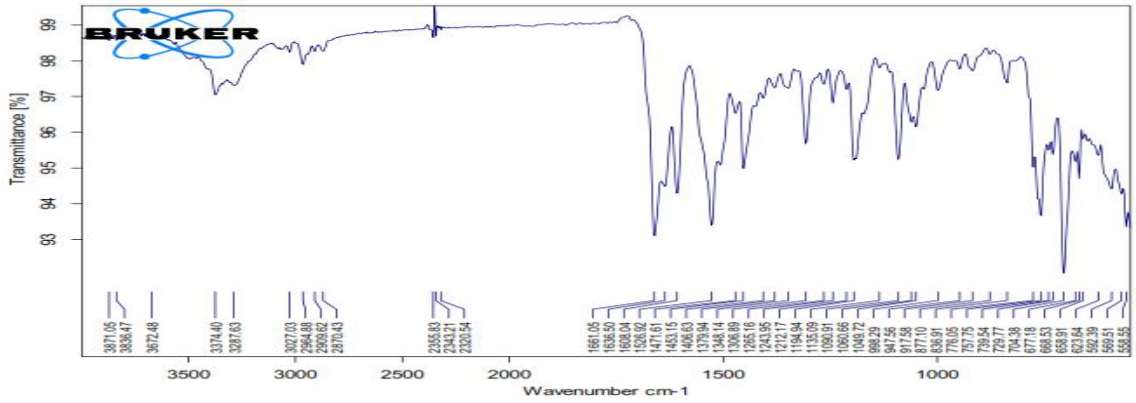

Fig: 8 FTIR Peak of pure drug Naratriptan

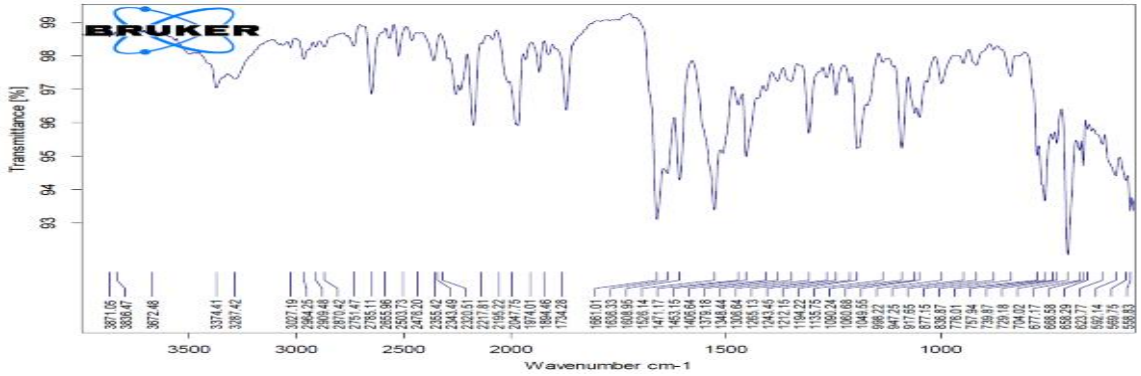

Fig:9 FTIR Peak of Optimized formulation

CONCLUSION:

The present study focused on the formulation development and evaluation of mucoadhesive buccal tablets of Naratriptan to enhance its bioavailability and provide a sustained release effect, bypassing hepatic first-pass metabolism. Various formulations were prepared using different concentrations and combinations of mucoadhesive polymers such as Sodium starch glycolate, Crospovidone and Croscarmellose sodium. All the prepared formulations were evaluated for pre-compression and post-compression parameters, and the results were found to be within acceptable limits as per IP specifications. Among all the formulations, F4 was identified as the optimized one based on its satisfactory drug content, mucoadhesive strength, swelling index, surface pH, and in vitro drug release profile, showing a sustained release up to 8 hours with a cumulative drug release of 99.72%.

Thus, the study successfully demonstrates that mucoadhesive buccal tablets of Naratriptan can be a promising alternative to conventional dosage forms for effective migraine management, providing prolonged therapeutic action with improved patient compliance.

REFERENCES:

1. V. T. Iswariya and A. Hari Om Prakash Rao. Buccal Tablets A Comprehensive Review. ejpmr, 2016,3(8), 252-262.
2. S.K.Gupta et al; Buccal adhesive drug delivery system: A review; Asian Journal Of Biochemical and pharmaceutical research, 2011;1(2): 105-114.
3. Reena Sheoran. Buccal Drug Delivery System: A Review. Int. J. Pharm. Sci. Rev. Res., 50(1), May - June 2018; Article No. 07, Pages: 40-46.
4. Wertz, P.W. and Squier, C.A., Cellular and molecular basis of barrier function in oral epithelium, Crit. Rev. Ther. Drug Carr. Sys, 8, 1991, 237-269.
5. Squier, C.A., Cox, P., and Wertz, P.W., Lipid content and water permeability of skin and oral mucosa, The J. Invest. Dermat, 96, 1991, 123-126.
6. Squier, C.A. and Wertz, P.W. Structure and function of the oral mucosa and implications for drug delivery, in eds. M.J. Rathbone, Oral Mucosal Drug Delivery, Marcel Dekker, Inc., New York, New York, 1996, 1-26.
7. Galey, W.R., Lonsdale, H.K., and Nacht, S., The in vitro permeability of skin and buccal mucosa to selected drugs and J Pharm Pharmaceut Sci (www.ualberta.ca/~csps) 1 (1), 1998, 15-30.
8. Gandhi, R.B. and Robinson, J.R., Oral cavity as a site for bioadhesive drug delivery, Adv. Drug Del. Rev., 13, 1994, 43-74.
9. Peppas, N.A. and Buri, P.A., Surface, interfacial and molecular aspects of polymer bioadhesion on soft tissues, J.Control. Rel., 2, 1985, 257-275.
10. Duchene D, Touchard F and Peppas N A Pharmaceutical and medical aspects of Bioadhesive system for drug administration. Drug Dev. Ind. Pharm.; 14, 1998, 283-381.
11. Parth S. Patel ,Ashish M. Parmar, Nilang S. Doshi, Hardik V. Patel, Raxit R. Patel, Chetan Nayee. Buccal Drug Delivery System: A Review.
12. Webster's Encyclopedic Unabridged Dictionary of the English Language. Thunder Bay Press, Avenel (NJ, USA), 2001.
13. Kaelbe D H and Moacanin J. A surface energy analysis of bioadhesion. Polym.; 18: 475-481, 1977.
14. Gu J M, Robinson J R and Leung S. binding of acrylic polymers to mucin/epithelial surfaces; Structure property-relationship. Crit. Rev. Ther. Drug Car. Sys.; 5, 21-67, 1998.
15. Duchene D, Touchard F and Peppas N A. Pharmaceutical and medical aspects of Bio adhesive system for drug administration. Drug Dev. Ind. Pharm.; 14, 283-381, 1998.
16. Hollingsbee D A and Timmins P. Topical adhesive system, in Bioadhesion Possibilities and Future Trends, Gurny R and Junginger H E Eds., Wissenchaftliche Verlag Gesellschaft, Stuttgart; 140-164, 1990.
17. R. Jagadeeshwar Reddy, Maimuna Anjum and Mohammed Asif Hussain. A Comprehensive Review on Buccal Drug Delivery System. AJADD [1][3][2013]300-312.
18. Wise Donald L, Handbook of Pharmaceutical controlled release technology: 255-265.
19. Magi. L. et. al., (1994), S.T.P. Pharma Sciences, 4(5), 343.
20. Jimenez-Castellannos MR. Zia. H., Rhodes CT., (1993), Drug Dev. Ind Phar., 19(142), 143.
21. www.controlled drugdelivery.com.
22. AP Gandhi; KR Patel; MR Patel; NM Patel. Int. J. Pharm. Res. Dev., 2011, 3(5), 159-173.
23. R Venkatalakshmi; S Yajaman; M Chetty; C Sasikala; M Varma. Int. J. Pharm. Sci. Res. 2012, 3(1), 35-41.
24. N Sharma; S Jain; S Sardana. J. Adv. Pharm. Edu. Res., 2013, 3(1), 1-15.
25. SK Gupta; IJ Singhavi; M Shirsat; G Karwani; A Agrawal; A Agrawal. Asian J. Biochem. Pharm. Res., 2011,2(1), 105-114.
26. GA Khairnar; FJ Sayyad. Int. J. Pharm. Tech. Res., 2010, 2(1), 719-735.
27. V Prajapati; M Bansal; PK Sharma. Int. J. Pharm. Tech. Res., 2012, 4(2), 582-589.
28. Gandhi SD, Pandya PR, Umbarkar R, Tambawala T and Shah MA. Mucoadhesive drug delivery system- an unusual maneuver for site specific drug delivery system, Inter. J. Pharm. Sci., 2011, 851- 872.

29. Patil SB, Murthy RSR, Mahajan HS, Wagh RD and Gattani SG. Mucoadhesive polymers: means of improving drug delivery, Pharm. Times, 2006, 38 (4), 25-28.
30. Shojaei Amir H, Buccal Mucosa as A Route for Systemic Drug Delivery: A Review; J Pharm Pharmaceut Sci (www.ualberta.ca/~csps) 1998;1 (1):15-3.
31. Horstedt P, Danielsson A, Nyhlin H, Stenling R and Suhr O. Adhesion of bacteria to the human small intestinal mucosa. Scandinavian J. Gastroenterology; 24, 877-885, 1989.
32. Peppas N A and Buri P A. Surface, interfacial and molecular aspects of polymer bioadhesion on soft tissues. J. Control. Release; 2, 257-275, 1985.
33. Woodley J. Bioadhesion: New Possibilities for Drug Administration. Clin. Pharmacokinetic.; 40(2), 77-84, 2001.
34. Harding SE, Davis SS, Deacon MP and Fiebrig I. Biopolymer mucoadhesive. Biotechnology. Genet. Eng. Rev.; 16, 41-86, 1999.
35. Keutscher A H, Zegarelli E V, Beube F E, Chiton N W. A new vehicle (Orabase) for the application of drugs to the oral mucus membranes, Oral Pathol.; 12, 1080-1089, 1959.
36. Chen J L and Cyr G N. Compositions producing adhesion through hydration, in Adhesion in Biological Systems, Manly R S Eds, Academic Press, New York, 163-167, 1970.
37. Nagai, Machida, Mucosal Adhesive Dosage Forms, Pharm., Int.196-200:1985.
38. Devarajan, P.V. and Adani, M.H., In; Jain, N.K., Eds, Controlled and Novel Drug Delivery, CBS Publishers and Distributors; New Delhi, India:2004, 52-81.
39. Gandhi, R.B., Robinson, J.R, Oral cavity as a Site for bio adhesive Drug Delivery, Adv. Drug Del. Rev.,13;43-74:1994.
40. N.R. Jimenez-Castellanos, H. Zia and C.T. Rhodes, Mucoadhesive drug Delivery Systems, Drug Dev. Ind. Pharm.19;143:1993.